(a) culturing a host cell under conditions suitable to produce a polypeptide encoded by the polynucleotide of claim 57, wherein said polynucleotide is (a), (b), (c) or (d); and

(b) recovering the polypeptide [protein].

Remarks

Claims 21-71 and 73-74 are pending in the instant application. The claims have been amended to more particularly point out and distinctly claim the subject matter Applicants regard as the invention. The amendments are supported in the claims as originally filed and throughout the specification. Thus, no new matter has been introduced.

I. Constructive Election.

The Examiner has withdrawn claims 55 and 56 from consideration as allegedly being drawn to a non-elected invention. (*See*, Paper No. 13, Pages 2-3.) In particular, the Examiner contends that "a composition comprising a DNA implies gene therapy as an intended use."

Applicants respectfully disagree and traverse the withdrawal of claims 55 and 56 from further consideration as allegedly being drawn to a non-elected invention. The Examiner contends that "a composition comprising a DNA implies gene therapy as an intended use," and then addresses the rejected claims as if they are directed to methods of gene therapy. Applicants respectfully point out that claims 55 and 56 are directed to compositions of matter and not methods. As such, Applicants assert that "divergent considerations and a search of additional classes/subclasses such as 424/93.1 and 514/44. . ." are not required for examination of composition of matter claims.

Even assuming *arguendo* that the Examiner's contention that a search of gene therapy as an intended use is proper, restriction remains improper unless it can be shown that the search and examination of both groups would entail a "serious burden". *See*, M.P.E.P. §

803. In the present situation, no such showing has been made. Indeed, no arguments have been made explaining why it would impose an undue burden to examine the proposed divergent considerations and additional classes/subclasses along with the classes/subclasses required for Group I. Applicants submit that a search of the polynucleotide claims of Group I would provide useful information for a search designed to encompass a potential use of the polynucleotides in gene therapy. For example, in many if not most publications reporting a gene therapy experiment, the authors also routinely include sequence-specific information regarding the polynucleotides used in the experiment. Thus, the searches for polynucleotides and the use of those polynucleotides in gene therapy commonly overlap. Thus, the search and examination of a polynucleotide and the use of those polynucleotides in gene therapy would not entail a serious burden.

Accordingly, as applied to claims 55 and 56, the constructive election of claims 21-54 and 57-75 should be withdrawn, and examination of all of claims 21-75 should be undertaken.

II. Information Disclosure Statement.

The Examiner has objected to the Information Disclosure Statement ("IDS") filed on October 28, 1999 because it allegedly fails to comply with 37 C.F.R. § 1.98(a)(3) by not "includ[ing] a concise explanation of the relevance, as it is presently understood by the individual designated in 37 C.F.R. 1.56(c) most knowledgeable about the content of the information, of each patent listed that is not in the English language." (*See*, Paper No. 13, Pages 3-4.)

Applicants assert that in the IDS filed on October 28, 1999, Applicants indicated that "[t]he relevance of Japanese language document (reference AE) can be found in the drawings." (*See*, Supplemental Information Disclosure Statement of October 28, 1999.) Applicants intended to indicate that the relevance of Japanese language document (reference AE) can be found in the two polypeptide sequences found at page 7 of reference AE (JP 10265498). Applicants submit herewith, for the Examiner's convenience, an alignment of

SEQ ID NO:2 of the instant application and the first polypeptide sequence presented on page 7 of reference AE (attached hereto as Exhibit 1). Applicants also submit herewith, for the Examiner's convenience, an alignment of SEQ ID NO:2 of the instant application and the second polypeptide sequence presented on page 7 of reference AE (attached hereto as Exhibit 2).

Applicants respectfully assert that the above explanation of the relevance of reference AE (*i.e.*, JP 10265498) satisfies Applicants' duty under 37 C.F.R. §§ 1.56 and 1.98(a)(3). Accordingly, Applicants respectfully request that the Examiner's objection to the IDS of October 28, 1999 be withdrawn and that the information referred to therein be considered.

III. Rejections of the Claims under 35 U.S.C. §112, First Paragraph.

A. Availability of the Deposited Material.

The Examiner has rejected claims 21, 46, 47, 57, and 75 under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to make and/or use the invention. Specifically, the Examiner contends that the deposit was made under the terms of the Budapest Treaty, however "it is not apparent whether the deposit is readily available to the public." (*See*, Paper No. 13, Pages 4-5.)

Applicants' representative hereby gives the following assurance by signature below:

Human Genome Sciences, Inc., an assignee of the present application, has deposited biological material under the terms of the Budapest Treaty on the International Recognition of the Deposit of Micro-organisms for the Purposes of Patent Procedure with the following International Depository Authority: American Type Culture Collection (ATCC), 10801 University Boulevard, Manassas, Virginia 20110-2209. This deposit comprises cDNA sequences encoding Tissue Plasminogen Activtor-Like Protease ("t-PALP"). The deposit for t-PALP was made on May 8, 1997, and given ATCC Accession Number 209023. In accordance with M.P.E.P. § 2410.01 and 37 C.F.R. § 1.808, assurance is hereby given that all restrictions on the availability to the public of ATCC Accession Number 209023 will be

irrevocably removed upon the grant of a patent based on the captioned application, except as permitted under 37 C.F.R. § 1.808(b). A copy of the ATCC Deposit receipt for Accession Number 209023 is enclosed herewith.

As a result, Applicants assert that the Examiner's rejection of claims 21, 46, 47, 57, and 75 under 35 U.S.C. § 112, first paragraph, is obviated by the statement regarding availability of the deposited material and the amendment correcting the present address of the ATCC. Therefore, Applicants respectfully request that the rejection be withdrawn.

B. "How to Use."

The Examiner has rejected claims 72-75 under 35 U.S.C. § 112, first paragraph, because the claim recites subject matter allegedly not "supported by either a specific asserted utility or a well established utility for the reasons set forth above [*i.e.*, in the rejection under 35 U.S.C. § 101], one skilled in the art clearly would not know how to use the claimed invention." (*See*, Paper No. 13, Page 6.)

Applicants respectfully disagree and traverse.

Applicants assert that nucleic acid molecules of the present invention are supported by both a credible asserted utility and a well-established utility. In the remarks below, directed to the Examiner's rejection under 35 U.S.C. § 101, Applicants point to several examples of specific, credible, and well-established utilities in the specification as originally filed. The specification teaches that t-PALP nucleic acid molecules are useful, for example, as hybridization probes for differential identification of the tissue(s) or cell type(s) present in a biological sample.

The test for enablement is whether one reasonably skilled in the art could make or use the invention from the disclosure in the patent coupled with information known in the art without undue experimentation. M.P.E.P. § 2164.01(a). Undue experimentation is experimentation that would require a level of ingenuity beyond what is expected from one of ordinary skill in the field. *Fields v. Conover*, 443 F.2d 1386, 1390-91, 170 USPQ

276, 279 (C.C.P.A. 1971). The test for undue experimentation is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine. *Id.*

Additionally, the Federal Circuit and its predecessor determined that the utility requirement of Section 101 and the how to use requirement of Section 112, first paragraph, have the same basis, *i.e.*, the disclosure of a credible utility. *See*, *In re Brana*, 51 F.3d 1560, 1564, 34 USPQ2d 1436, 1441 (Fed. Cir. 1995); *see also*, *In re Jolles*, 628 F.2d 1322, 1326 n.11, 206 USPQ 885, 889 n. 11 (CCPA 1980); and *In re Fouche*, 439 F.2d 1237, 1243, 169 USPQ 429, 434 (CCPA 1971).

As discussed *infra*, the specification teaches specific and well established utilities of the claimed nucleic acid molecules. The specification teaches that the claimed nucleic acid molecules have a variety of practical and immediate uses, for example, identifying tissue type and origin, chromosome mapping or labeling, locating disease-associated genes on the chromosome, etc. Thus, the specification asserts several specific and immediate utilities, thereby enabling the skilled artisan to use the claimed nucleic acid molecules.

The Examiner states that due to the large number of sequences embraced by the claims and the alleged lack of adequate guidance as to how to use the claimed sequences, the claims do not meet the requirements of 35 U.S.C. § 112, first paragraph. However, that the claims encompass a significant number of sequences does not negate patentability. In *Amgen v. Chugai* (927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir. 1991)), the claim at issue related to DNA sequences encoding erythropoietin (EPO) and biologically active analogs thereof. The court focused on the lack of guidance to one skilled in the art to make DNA sequences that had the recited utility, *i.e.*, encoded a biologically active EPO analog. *Amgen*, 927 F.2d at 1214, 18 USPQ2d at 1028. In view of such a lack of guidance, the Federal Circuit found that the claims were not enabled. *Amgen*, 927 F.2d at 1214, 18 USPQ2d at 1028. The court's analysis of enablement focused specifically on Amgen's lack of guidance rather than the large number of sequences encompassed by the claims.

Accordingly, in the present case, the utility of the nucleic acid molecules encompassed by the claims is specific, and the present specification as originally filed

teaches how to use polynucleotides that possess the recited utilities. Because the test for enablement focuses on guidance, and not necessarily on the number of species, the number of nucleic acid molecules encompassed by the claims is legally irrelevant. Therefore, the claimed nucleic acid molecules are fully enabled.

Because the present invention is supported by both credible and well-known uses, one of ordinary skill in the art would immediately know how to use the claimed invention. Moreover, because the specification teaches how to use the claimed nucleic acid molecules with only routine experimentation and the specification describes specific and immediate utilities for the claimed nucleic acid molecules, Applicants submit that the full scope of the claims is enabled. Accordingly, Applicants respectfully request that the rejection of the pending claims under 35 U.S.C. § 112, first paragraph, be withdrawn.

IV. Rejection of the Claims under 35 U.S.C. § 101.

The Examiner has rejected claims 72-75 under 35 U.S.C. § 101 because the invention is allegedly not supported by either a specific asserted utility or a well established utility. (*See*, Paper No. 13, Pages 5-6.) Applicants have canceled claims 72 and 75 thereby obviating any rejection of these claims. Thus, Applicants respond to the rejection as it applies to claims 73 and 74. In this regard, the Examiner contends that because nucleic acid molecules encompassed by the rejected claims are not limited in length to 30 and 50 nucleotides of a specifically recited fragment of SEQ ID NO:1 of the instant application, that the rejected claims "encompass countless number of sequences with an unknown function." Moreover, the Examiner contends that "[t]here is no guidance presented as to what is the specific function of the sequences."

Applicants respectfully disagree and traverse.

A rejection under 35 U.S.C. § 101 is improper when a person of ordinary skill in the art would find credible disclosed features or characteristics of the invention made by the Applicant in the written description of the invention. M.P.E.P. § 2107.01(II)(B) at 2100-37. In addition, an Applicant need only make one credible assertion of specific utility

for the claimed invention to satisfy 35 U.S.C. § 101; additional statements of utility, even if not "credible," do not render the claimed invention lacking in utility. *See, e.g., Raytheon v. Roper*, 724 F.2d 951, 958, 220 U.S.P.Q. 592, 598 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 835 (1984) ("When a properly claimed invention meets at least one stated objective, utility under 35 U.S.C. § 101 is clearly shown."). Thus, if Applicant makes one credible assertion of utility, utility for the claimed invention as a whole is established. M.P.E.P. § 2107.01(I) at 2100-36. Further, finding a lack of utility is also improper if a person of ordinary skill in the art would know of a use for the claimed invention at the time the application was filed. M.P.E.P. § 2107.01(II)(B) at 2100-37.

Contrary to the Examiner's assertions, Applicants respectfully submit that nucleic acid molecules comprising 30 or 50 contiguous nucleotides of the specific fragment recited in the rejected claims possess one or more of the same utilities that characterize the full-length, full-length minus the amino-terminal methionine residue, the mature form, and other t-PALP nucleic acid molecules. Such utilities are specifically asserted and well-established and one of ordinary skill in the art would find these utilities credible. Full-length, full-length minus amino-terminal methionine, mature nucleic acid molecules, as well as nucleic acid molecules comprising 30 or 50 contiguous nucleotides of the fragment recited in the rejected claims of the present invention may be used, for example, as hybridization probes for differential identification of the tissue(s) or cell type(s) present in a biological sample; for detecting expression of the t-PALP gene in human tissue, for instance, by Northern blot analyses; as probes for isolating other related molecules known to encode useful polypeptides, *e.g.*, homologs such as t-PA, or variants of t-PALP or t-PA; as probes of the invention to screen genomic DNA libraries to isolate sequences that reside in the same chromosomal region as the t-PALP gene; as probes for *in situ* hybridization; and as probes for specifically labeling human chromosomes. (*See e.g.*, specification, at page 6, lines 1-4, and at page 8, line 33 through page 9, line 4; at page 12, lines 3-7; at page 56, lines 7-25 (*i.e.*, Example 4); at page 49, line 28 through page 50, line 5; at page 12, lines 4-6; and at page 44, line 27 through page 45, line 23.)

Applicants respectfully submit therefore that nucleic acid molecules comprising 30 or 50 contiguous nucleotides of the presently claimed invention possesses a credible, well-established utilities, as indicated above, that constitute patentable utilities under 35 U.S.C. § 101. Therefore, Applicants' assertions of utility are sufficient to satisfy the requirements of 35 U.S.C. § 101. Accordingly, Applicants respectfully request that the Examiner's rejection of claims 73 and 74 under 35 U.S.C. § 101 be reconsidered and withdrawn.

V. Rejection of the Claims under 35 U.S.C. §112, second paragraph.

The Examiner has rejected claim 69 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. (*See*, Paper No. 13, Pages 6-7.) In particular, the Examiner contends that, while Applicant may be his or her own lexicographer, a term in a claim may not be given a meaning repugnant to the usual meaning of the term. The Examiner further contends that "[a]ccording to the US Patent Classification System (class 530/350), the term 'protein' encompasses more than 100 amino acid residues."

Applicants respectfully disagree and traverse.

Applicants assert that one of ordinary skill in the art would understand that a molecule may comprise 100 or less amino acid residues and still be designated a "protein." However, solely in the interest of facilitating prosecution, Applicants have amended claim 69 to delete reference to the term "protein" and to insert reference to the term "polypeptide." Applicants Assert that the Examiner's concern has been addressed and that the rejection has been obviated. Therefore, Applicants respectfully request that the rejection of claim 69 under 35 U.S.C. § 112, second paragraph, be withdrawn.

VI. Rejection of the Claims under 35 U.S.C. §102.

A. Rejection over Du, et al., Hudson (a), Hudson (b) or Adams under 35 U.S.C. § 102(a).

The Examiner has rejected claims 21-54 and 57-71 under 35 U.S.C. § 102(a) as allegedly being anticipated by Du, et al., Hudson (a), Hudson (b) or Adams. (*See*, Paper No. 13, Page 7.) In particular, the Examiner contends that because "claims 21(e) and 57(e) are not limited to a full-length sequences (sic), any of the Du et al., Hudson (a), Hudson (b) or Adams sequences anticipate a nucleic acid molecule recited in claims 21(e) and 57(e)."

Applicants respectfully disagree and traverse.

In order for a reference to anticipate a claim, each and every element of the claim must be disclosed in that one reference. *Orthokinetics, Inc. v. Safety Travel Chairs, Inc.*, 1 U.S.P.Q.2d 1081 (Fed. Cir. 1985). Applicants assert that claims 21(e) and 57(e) are not intended to be limited to a "full-length" sequence, and are not required to be limited to a "full-length" sequence in order to overcome the cited references. The Examiner has not rejected claims 21(a), (b), (c) or (d) or claims 57(a), (b), (c) or (d) over the cited references. Therefore, the Examiner's concern is apparently directed to the interpretation of recitation (e) of claims 21 and 57 wherein the phrase "a nucleic acid complementary to any of the nucleic acids in (a), (b), (c) or (d), above" means "a nucleic acid complementary to any <u>fragment</u> of the nucleic acids in (a), (b), (c) or (d), above." However, by recitation (e) of claims 21 and 57, Applicants intend only that the nucleic acid claimed therein comprises a nucleic acid molecule that is fully complementary to the nucleic acid molecule in recitations (a), (b), (c) or (d) of claims 21 or 57. Applicants have amended recitation (e) claims 21 and 57 accordingly to insert the word "fully."

Because claims 21 and 57 have been amended to address the Examiner's concerns, Du et al., Hudson (a), Hudson (b) or Adams cannot anticipate the claims. Accordingly, Applicants respectfully request that the rejection of claims 21-54 and 57-71 under 35 U.S.C. § 102(a) be withdrawn.

B. Rejection over Hillier, et al. (a) or Hillier, et al. (b) under 35 U.S.C. § 102(b).

The Examiner has rejected claims 21-54 and 57-71 under 35 U.S.C. § 102(b) as allegedly being anticipated by Hillier, et al. (a) or Hillier, et al. (b). (*See*, Paper No. 13, Page 8.) In particular, the Examiner contends that because "claims 21(e) and 57(e) are not limited to a full-length sequences (sic), any of the Hillier et al. (a) or Hillier et al. (b) sequences anticipate a nucleic acid molecule recited in claims 21(e) and 57(e)."

Applicants respectfully disagree and traverse.

In order for a reference to anticipate a claim, each and every element of the claim must be disclosed in that one reference. *Orthokinetics, Inc. v. Safety Travel Chairs, Inc.*, 1 U.S.P.Q.2d 1081 (Fed. Cir. 1985). Applicants again assert that claims 21(e) and 57(e) are not intended to be limited to a "full-length" sequence, and are not required to be limited to a "full-length" sequence in order to overcome the cited references. The Examiner has not rejected claims 21(a), (b), (c) or (d) or claims 57(a), (b), (c) or (d) over the cited references. Therefore, the Examiner's concern is apparently directed to the interpretation of recitation (e) of claims 21 and 57 wherein the phrase "a nucleic acid complementary to any of the nucleic acids in (a), (b), (c) or (d), above" means "a nucleic acid complementary to any fragment of the nucleic acids in (a), (b), (c) or (d), above." However, by recitation (e) of claims 21 and 57, Applicants intend only that the nucleic acid claimed therein comprises a nucleic acid molecule that is fully complementary to the nucleic acid molecule in recitations (a), (b), (c) or (d) of claims 21 or 57. Applicants have amended recitation (e) claims 21 and 57 accordingly to insert the word "fully."

Because claims 21 and 57 have been amended to address the Examiner's concerns, Hillier, et al. (a) or Hillier, et al. (b) cannot anticipate the claims. Accordingly, Applicants respectfully request that the rejection of claims 21-54 and 57-71 under 35 U.S.C. § 102(b) be withdrawn.

Conclusion

Entry of the above amendment is therefore respectfully solicited. In view of the foregoing remarks, Applicants believe that this application is now in condition for allowance. An early notice to that effect is urged. The Examiner is invited to call the undersigned at the phone number provided below if any further action by Applicant would expedite the examination of this application.

Finally, if there are any fees due in connection with the filing of this paper, please charge the fees to our Deposit Account No. 08-3425. If a fee is required for an extension of time under 37 C.F.R. § 1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account.

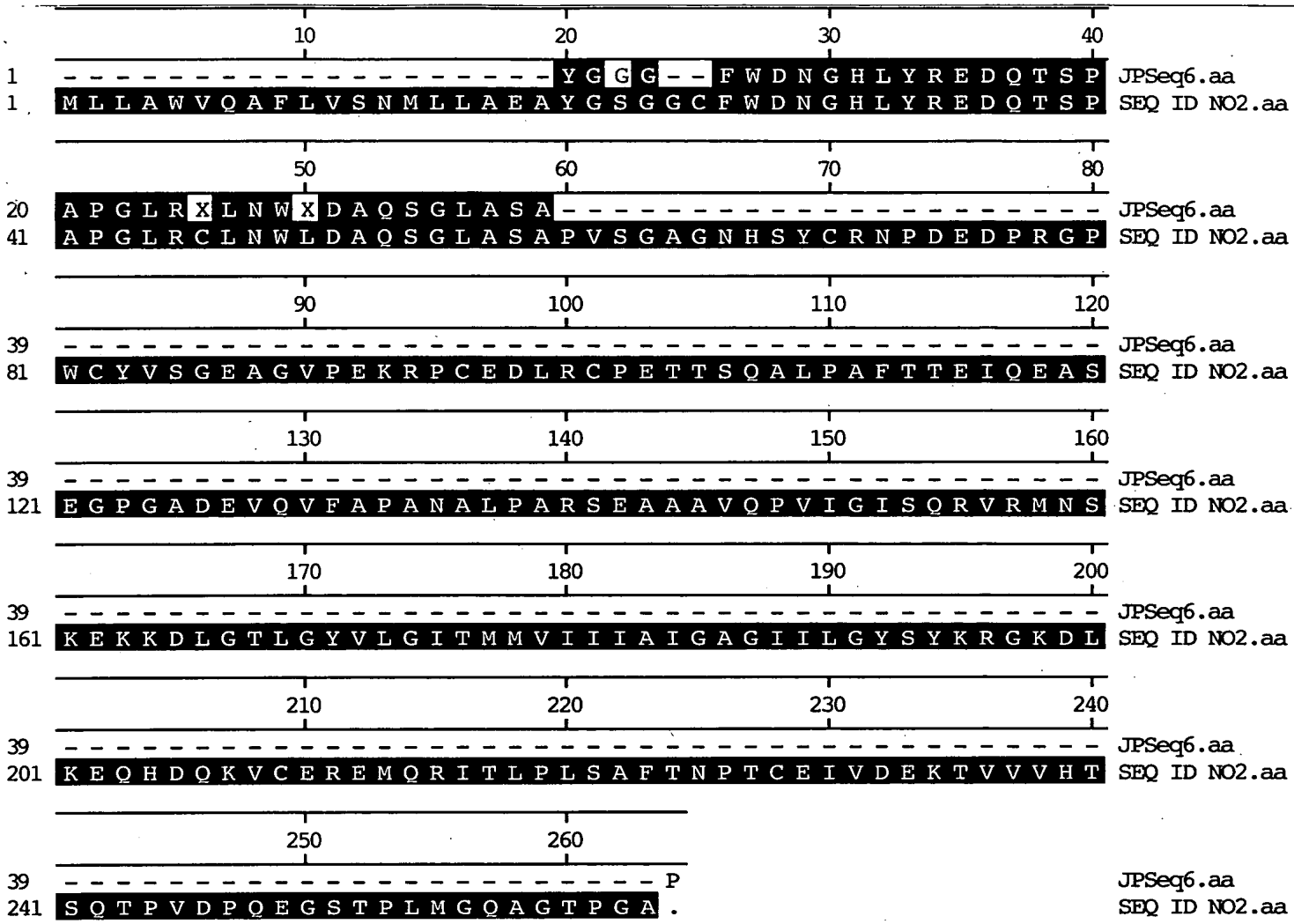
Respectfully submitted,

Dated: April 20, 2000

Joseph J. Kenny (Reg. No. 43,710)
Agent for Applicants

Human Genome Sciences, Inc.
9410 Key West Avenue
Rockville, MD 20850
Telephone: (301) 610-5800

Enclosures
MMW/JJK/lcc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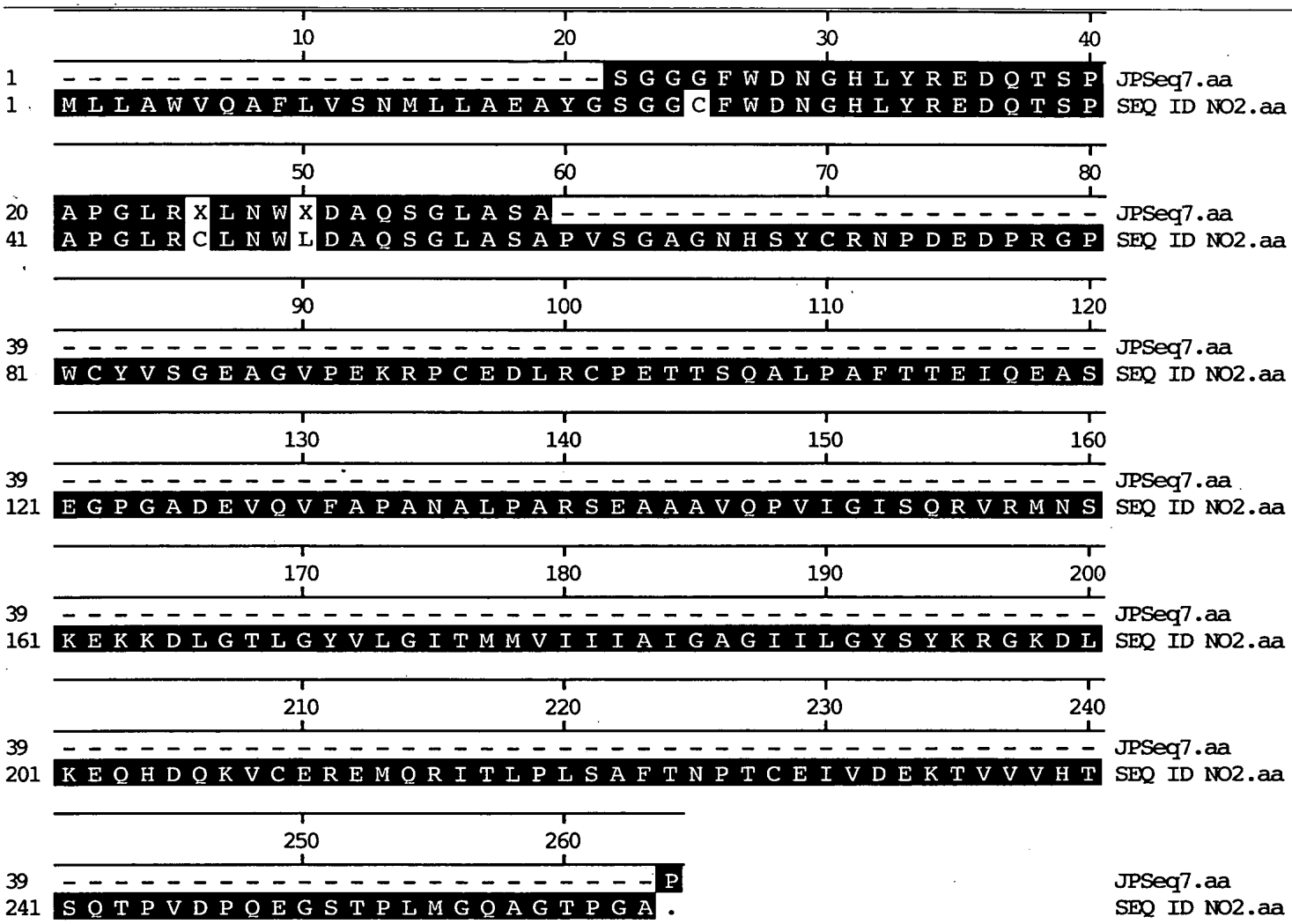
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BUDAPEST TREATY ON THE INTERNATIONAL RECOGNITION OF
THE DEPOSIT OF MICROORGANISMS FOR THE PURPOSES OF PATENT PROCEDURE

INTERNATIONAL FORM

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT ISSUED PURSUANT TO RULE 7.3
AND VIABILITY STATEMENT ISSUED PURSUANT TO RULE 10.2

MAY 1 0 1997

HGS PATENT DEPT.

To: (Name and Address of Depositor or Attorney)

Human Genome Sciences, Inc.
Attn: Robert H. Benson
9410 Key West Avenue
Rockville, MD 20850

Deposited on Behalf of: Human Genome Sciences, Inc. (Docket Nos. PS029 and PF378)

Identification Reference by Depositor:	**ATCC Designation**
DNA plasmid PS029	209022
DNA Plasmid HMS1B42	209023 ✓

The deposits were accompanied by: __ a scientific description _a proposed taxonomic description indicated above.

The deposits were received May 8, 1997 by this International Depository Authority and have been accepted.

AT YOUR REQUEST:

X We will inform you of requests for the strains for 30 years.

The strains will be made available if a patent office signatory to the Budapest Treaty certifies one's right to receive, or if a U.S. Patent is issued citing the strains, and ATCC is instructed by the United States Patent & Trademark Office or the depositor to release said strains.

If the cultures should die or be destroyed during the effective term of the deposit, it shall be your responsibility to replace them with living cultures of the same.

The strains will be maintained for a period of at least 30 years from date of deposit, or five years after the most recent request for a sample, whichever is longer. The United States and many other countries are signatory to the Budapest Treaty.

The viability of the cultures cited above was tested May 15, 1997. On that date, the cultures were viable.

International Depository Authority: American Type Culture Collection, Rockville, Md. 20852 USA

Signature of person having authority to represent ATCC:

Barbara M. Hailey

Barbara M. Hailey, Administrator, Patent Depository

Date: May 15, 1997